Association of Retinal Vascular Diameter and Vascular Branching Angle with Diabetic Retinopathy Stage: 
A Cross-Sectional Study

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Abstract

Purpose: To determine the association between retinal vascular diameter and its branching angles with diabetic retinopathy (DR) stages in diabetic patients

Methods: A descriptive analytic cross-sectional study was conducted in 62 diabetic patients (120 eyes) referred to Farabi Eye Hospital between June 2008 and December 2009. Digital fundus photography pictures were imported into Photoshop software and diameters of arterioles and venules at their second branches from the disc were calculated. Meanwhile branching angles were measured in the same arterioles and venules. DR was graded by retinal specialists according to Airlie House classification of DR. Retinal vascular diameters and their branching angles were compared in different DR stages.

Results: There was a significant difference between retinal vascular diameters in different retinopathy stages. The diameter was significantly more in proliferative stage compared with mild nonproliferative stage (P<0.05). After multivariate analysis, age or hypertension has had no effect on the results. However, there was no significant difference between vascular angles in different retinopathy stages (P>0.05).

Conclusion: Retinal vascular diameter, but not retinal vascular angle, seems to be related with retinopathy stage regardless of age and hypertention in these patients.

Keywords: Diabetic Retinopathy, Vascular Angle, Vascular Diameter


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Introduction

Diabetes mellitus (DM) is a major health problem in today's industrial society with a prevalence of 7.7% in general population of Iran according to 2005 statistics.\(^1\) The resultant complications of this disease decrease the patients' quality of life. Diabetic retinopathy (DR), one of the complications of DM, is the most common cause of newly developed blindness among patients aged 20 to 74 years old in western countries.\(^2,3\) Risk of developing blindness in diabetic patients is 25 times more than the normal population.\(^2\)

Although having a sight-threatening lesion in their retinas, most of the patients do not complain of any symptoms.\(^2\)

Based on various statistics, the prevalence of DR varies from 6.7% to 35%.\(^4,5\) Almost all patients with type I DM and more than 60% of patients with type II DM develop retinopathy during the first two decades of the disease.\(^6\)

Population-based studies and clinical trials demonstrated risk factors of DR, such as longer duration of diabetes, poorer glycemic control and elevated blood pressures which are shown to be major risk factors not only for developing DR, but also for progression of the existing retinopathy.\(^7\)

Current studies have shown that retinal venular and arteriolar caliber are among the factors undergoing major changes in patients with DR, not making clear if these changes are of prognostic values; controversial results are reported in some of these studies.\(^8-12\)

As a result, this study aimed to evaluate if retinal vascular caliber and their angle of branching were associated with severity of retinopathy in diabetic patients referred to a tertiary referral hospital.

Methods

In a descriptive analytic cross-sectional study, 62 patients (120 eyes) suffering from DR referred to a tertiary referral hospital were examined between June 2008 and December 2009. Patients with major media opacities, history of previous panretinal photocoagulation, intravitreal injection of triamcinolone or bevacizumab, intraocular inflammation, uncontrolled intraocular pressure, epiretinal membrane, severe and clinically apparent tractions or history of vitreoretinal surgeries were not included in the study. The study protocol was approved by the Institutional Ethics Committee of the Tehran University of Medical Sciences. After obtaining written informed consent, 30 degree digital infrared (IR) images taken by HRAII (Heidelberg retinal angiogram II, Heidelberg engineering, Germany) of six fields were taken through dilated pupils for each eye following a standardized protocol.\(^13,14\) The images were imported into Photoshop software version CS3 and retinal arteriolar and venular calibers were measured at 8 points between their second and third branching at superotemporal and inferotemporal fields (Figures 1-3). All of the measurements were done by a single operator from the outer border of each vessel under magnification and using the number of pixels occupied by diameter of the vessel. Number of pixels was converted to micrometer by using a coefficient from a standard image. Angle of branching were also measured on the same IR images imported into Photoshop at their second branching from optic disc at superotemporal and inferotemporal fields. Mean of measurements in each field was used for next analysis.

DR was graded according to the Early Treatment Diabetic Retinopathy Study (ETDRS) adaptation of the modified Airlie House classification of DR as mild, moderate, severe and very severe nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).\(^15\)

Using a check list, demographic data were collected including age, sex, duration of diabetes and the type of treatment used (oral agents or insulin). Measurement of blood pressure (including positive history for hypertension) and blood sugar was done. The recorded caliber of superior and inferior arteries and veins and their angle of branching were added to the same list.

The data were analyzed using SPSS 13.0 for Windows software program, (SPSS Inc., Chicago, IL, USA). Pearson chi-square test, analysis of variances, Scheffe test and logistic regression test were used for statistical analysis when appropriate. A \(P<0.05\) was considered statistically significant.
Results

A total of 62 patients were included in the study (120 eyes, 53 of which were from males and 67 from females) with a mean age of 63.74±8.39 years and a mean diabetes duration of 16.04±6.87 years. Age and diabetes duration were significantly associated with DR stages; mean age and mean diabetes duration were respectively higher in mild NPDR and severe NPDR stages (P<0.05). Thirty-seven eyes (30.8%) were related to patients under insulin therapy and 83 eyes (69.2%) belonged to patients using oral agents; a greater rate of PDR was observed in patients under insulin therapy (P<0.05). Hypertension was documented in 64 eyes (53.3%) and PDR was more reported in hypertensive patients (P<0.05). PDR was reported in 38 (31.7%), mild NPDR in 28 (23.3%), moderate NPDR in 26 (21.7%), severe NPDR in 24 (20%) and very severe NPDR in 4 eyes (3.3%). The number of left and right eyes was equal; stage of retinopathy was not statistically related to the side affected.

The recorded mean±SD of vascular diameters were as follow (in µm): superior temporal artery, 93.0±20.3; inferior temporal artery, 92.4±20.3; superior temporal vein, 127.9±33.3; inferior temporal vein, 129.8±34.2. The angle of branchings was measured as follow (in degree): superior temporal artery, 84.2±18.4; inferior temporal artery, 83.6±18.3; superior temporal vein, 75.9±19.2; inferior temporal vein, 76.5±16.4. Detailed data for each ETDRS group are shown in Table 1.

There was a statistically significant difference between mean venular and arterial diameter in different stages of DR (P<0.05); however, there was no significant difference between moderate, severe and very severe NPDR or between each and PDR but there was a statistically significant difference in arteriolar and venular diameter between mild NDPR and PDR stages (having more diameters in PDR stage). After multivariate analysis, controlling for age, sex, and hypertension there was no difference in the results.

No significant difference was observed in arteriolar and venular branching angles between different stages of DR (P>0.05).
Table 1. Mean±SD of diameter (in micron) and branching angle (in degree) of vessels in different Early Treatment Diabetic Retinopathy Study groups

<table>
<thead>
<tr>
<th></th>
<th>Superior artery</th>
<th>Inferior artery</th>
<th>Superior vein</th>
<th>Inferior vein</th>
</tr>
</thead>
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<tr>
<td>Mild NPDR</td>
<td>Diameter</td>
<td>82.5±18.4</td>
<td>82.1±16.8</td>
<td>107.3±22.3</td>
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<td></td>
<td>Angle</td>
<td>83.7±23.0</td>
<td>84.6±21.6</td>
<td>78.1±18.7</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>Diameter</td>
<td>97.5±19.9</td>
<td>97.5±20.2</td>
<td>143.7±34.1</td>
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<tr>
<td></td>
<td>Angle</td>
<td>89.2±13.6</td>
<td>82.4±16.2</td>
<td>89.1±18.1</td>
</tr>
<tr>
<td>Severe NPDR</td>
<td>Diameter</td>
<td>102.4±18.7</td>
<td>101.9±20.6</td>
<td>136.9±28.0</td>
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<tr>
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<td>Angle</td>
<td>85.6±8.8</td>
<td>84.7±20.5</td>
<td>80.7±15.6</td>
</tr>
<tr>
<td>Very Severe NPDR</td>
<td>Diameter</td>
<td>100.2±15.3</td>
<td>106.2±9.7</td>
<td>144.4±11.4</td>
</tr>
<tr>
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<td>Angle</td>
<td>77.9±20.4</td>
<td>88.6±13.3</td>
<td>83.6±20.2</td>
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<tr>
<td>PDR</td>
<td>Diameter</td>
<td>90.9±20.1</td>
<td>89.1±19.7</td>
<td>124.7±36.4</td>
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<tr>
<td></td>
<td>Angle</td>
<td>80.9±16.8</td>
<td>82.4±16.6</td>
<td>68.2±20.9</td>
</tr>
</tbody>
</table>

NPDR: Nonproliferative diabetic retinopathy
PDR: Proliferative diabetic retinopathy

Discussion

In the present study by measuring retinal vascular diameter and its branching angles, it is considered that retinal arteriolar and venular diameter were associated with severity of DR, suggesting such a relationship in the general diabetic population. However, no association was found between retinal vascular branching angle and severity of DR. The findings remained the same after controlling for the probable confounders (age, sex, diabetes duration, type of treatment and hypertension).

In the Multi-Ethnic Study of Atherosclerosis (MESA), it was found that retinal arteriolar and venular diameter were greater in diabetic patients and retinal venular diameter was associated with DR signs.\(^8\) The Wisconsin Epidemiological Study for Diabetic Retinopathy (WESDR), just including type 1 diabetic patients, showed that a larger venular diameter was associated with severity of DR\(^9,10\). Nevertheless, Alibrahim et al concluded that retinal venular diameter was not associated with early DR; however they indicated a significant association between retinal arteriolar diameter and early DR.\(^11\) Cheung et al have shown that greater retinal fractal dimension (representing increased geometric complexity of the retinal vasculature) is independently associated with early DR signs in type 1 diabetes.\(^16\) The findings of our study, however cross-sectional, were in some part compatible with these findings. In our study it has been shown that patients with mild NPDR have narrower vessels compared with more advanced DR. One explanation would be different autoregulatory mechanisms working in diabetic patients that take action in cases of more advanced DR and other aggravating factors such as hyperperfusion, tissue hypoxia and ischemia may be involved in the process.\(^12,17-19\) Up to our knowledge, this study was the first one that simultaneously measured retinal vascular diameter with their branching angles. It showed that changes in vascular diameter were not associated with changes in branching angles.

Other factors such as systemic factors and even different treatments may have some effects in vascular diameter. Mendrinos et al have shown that panretinal photocoagulation has a vasoconstrictive effect on retinal arterioles in patients with severe nonproliferative or proliferative DR and it may be due to autoregulatory response of the retinal circulation to increased inner retinal oxygen tension.\(^20\) In another study intravitreal triamcinolone(IVTA) has had a significant
narrowing effect on both retinal arteriolar and venular diameter in eyes with diabetic macular edema.  
Grusland et al in their study have shown that in type 1 diabetic patients, retinal arteriolar narrowing is associated with nephropathy and macrovascular disease and it can be used as an indicator of vascular involvement in other organs.  
Our patients have had no history of panretinal photocoagulation or intravitreal injections. On the other hand multiple logistic regression has shown that factors such as hypertension are not responsible for difference in vascular diameter. 
There was no association found between the branching angle of retinal vessels and stages of DR. We did not find any other study considering these angles as a prognostic factor of DR.

This cross-sectional study lacks the accuracy of a comparative study in population-based settings; and low number of patients in some of our groups results in some limitations for our study, more studies with greater sample sizes seem necessary to confirm these findings.

**Conclusion**
Severity of DR is associated with increase in retinal vascular diameter, but not retinal vascular branching angles. As a result, the diameter of retinal vessels might be an indicator of the stage of DR; however, further studies are required.

### References